Case Report

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Test dosing as an alternative treatment approach in urinary tract infection patient with Cefoperazone allergy

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ABSTRACT

Drug hypersensitivity reaction (DHR) is classified as adverse reaction which is based on immunologic mediated reaction. Antibiotics are the most frequently prescribed drugs given to patients to treat bacterial infections, but also cause adverse drug reactions due to hypersensitivity in patients. We present here a case of cefoperazone drug allergy in a 75 years old patient with urinary tract infection requiring the test dosing approach.

Keywords: Drug hypersensitivity reaction, Test dosing, Urinary tract infection, Cefoperazone, Drug allergy

INTRODUCTION

Drugs can induce adverse reaction which is based on immunologic mediated reaction that, together with non-allergic direct mast-cell mediated DHRs, count for around 15% of all adverse drug reactions. Only when a definite immunological mechanism (either clinically significant drug-specific IgE or IgG antibodies or T cells, immediate or delayed hypersensitivity reaction) is demonstrated, these reactions should be classified as drug allergic reactions. ²⁻⁴

Antibiotics are the most frequently prescribed drugs given to patients to treat bacterial infections and reduce bacterial growth, one of which is in patients with urinary tract infections. Cephalosporins are one of the drugs used in the treatment of urinary tract infections, including cefoperazone. Although effective against pathogenic bacteria, cefoperazone can cause adverse drug reactions due to hypersensitivity in patients. DHR may prevent some patients from receiving this treatment. Patients with true DHR need to be identified and treated immediately as they can experience life-threatening complications from the interfering drug. Test dosing is the way to investigate diagnosis of DHR. T.8

CASE REPORT

A 75-year-old man was admitted to the wangaya hospital with a diagnosis of urinary tract infection. Initially he complained of fever for 3 days before being admitted to the hospital and bedrest during that time. There is a decrease in appetite and cough, accompanied by pain when urinating. During the history, he denied any history of drug allergy.

The patient exhibits optimal overall condition with stable hemodynamics. The urinalysis examination was carried out with positive bacterial results accompanied by the presence of flat cell leukocytes and epithelium, 75 leu/uL leukocyte esterase, protein +1, ketone +3, birilubin +1, and blood +2.

At the time of admission, the patient was given cefoperazone therapy 1 g every 12 hours by intravenous infusion. After 1 hour there was an allergic reaction to the drug in the form of erythema macules on the body with pruritus (Figure 1). The cefoperazone administration was immediately stopped and gave 4 mg of methylprednisolone orally twice a day and loratadine 10 mg once a day for 3 days of treatment.



Figure 1: Adverse reaction (macula erythema with pruritus).

Before being given test dosing, the patient's condition was stable (no signs and symptoms of DHR). The patient received test dosing therapy with levofloxacin with IV fluids (Ringer's lactate) with an accumulation time of 120 minutes starting from the lowest dose of levofloxacin 50 mg (10 drops per minute). Administration of the drug was observed and the dose was increased every 30 minutes to 125 mg (20 drops per minute) and 250 mg (30 drops per minute). Administration of levofloxacin up to a maximum dose of 500 mg (40 drops per minute) as shown in Table 1.

Test dosing result was considered positive because there were some symptoms or signs of an immediate DHR (pruritus) at about 90 min after the first dose was administered. Test dosing determined the offending drug and the safety and optimal under-threshold dose. The safe and optimal under-threshold dose of levofloxacin on test dosing was one step below the dose on step 4 when DHR occurred. The dose was 250 mg levofloxacin (40 drops per minute).

Table 1: Drug provication test of levofloxacin (intravenous infusion).

Step	Time (minute)	Cumulative time (minute)	Dosage (mg)	Infusion drops (per minute)
1	0	0	50	10
2	30	30	125	20
3	30	60	250	30
4	30	90	500	40
5	30	120 (Total 2h)	250	40

DISCUSSION

Drug hypersensitivity reactions can become manifest in a great variety of clinical symptoms and diseases, some of which are quite severe and even fatal. Antibiotics are the drugs most frequently causing them. The risk of sensitization and the severity of clinical symptoms depend on the dose and duration of treatment, the state of immune activation of the individual, and also the immunogenetic predisposition.

Cephalosporins are a class of antibiotics commonly prescribed in inpatient settings.¹¹ As many as 0.2-3% of patients reported having an allergic reaction to this drug.¹² Similar to this case, an allergic reaction occurred in the patient in the form of red and itchy spots after taking a cephalosporin drug, cefoperazone. Therefore, patients are given test dosing using other drugs.

Test dosing comes at the end of a step-wise approach in the drug allergy work-up. ¹³ It has the advantage of reproducing the allergic symptoms and any other adverse clinical manifestations regardless of the underlying mechanism. It is generally accepted as the "gold standard" investigation for the diagnosis of drug hypersensitivity. ^{14,15}

Test dosing can be given by injection, intravenous infusion or oral. 3,16 In this case, levofloxacin is given by IV fluids from the lowest dose of 50 mg (10 drops per minute). Every 30 minutes the dose is increased slowly to see the drug reaction arising at certain doses. 17 Administration of the first 90 minutes at a dose of 500 mg, the drug causes an itchy reaction. Therefore, the safe threshold for this case is 250 mg (40 drops per minute). Levofloxacin is a quinolone class drug, a highly effective synthetic antibiotic and one of the most commonly prescribed antibiotic classes in acute care hospital settings. It is indicated for use in urinary tract infections. 18

CONCLUSION

Medicines can cause opposite reactions, including antibiotics. Chronologic anamnesis and proper examination is needed in DHR. To get the usual dose, test dosing is necessary so that drugs can be given in accordance with the patient's condition.

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